

WE CLAIM:

1. A method of treating a Pervasive Developmental Disorder, comprising administering to a patient in need of such treatment an effective amount of a

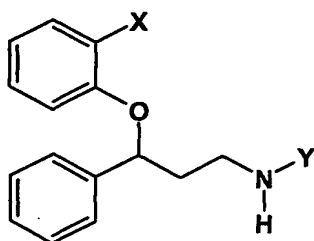
5 norepinephrine reuptake inhibitor selected from the group consisting of:

atomoxetine or a pharmaceutically acceptable salt thereof;

racemic reboxetine or a pharmaceutically acceptable salt thereof;

(S,S) reboxetine or a pharmaceutically acceptable salt thereof;

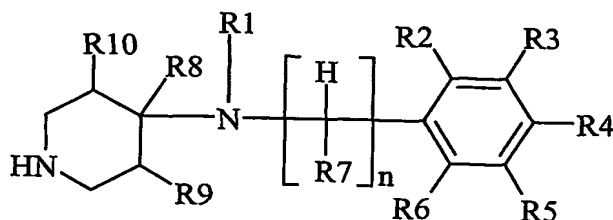
a compound of formula (I):



(I)

wherein X is C₁-C₄ alkylthio, and Y is C₁-C₂ alkyl, or a pharmaceutically acceptable salt thereof;

15 a compound of formula (IA):



(IA)

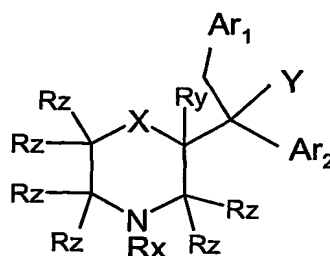
wherein n is 1, 2 or 3; R₁ is C₂-C₁₀alkyl, C₂-C₁₀alkenyl, C₃-C₈cycloalkyl or C₄-C₁₀cycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally substituted by an O-C or C=C bond and wherein each group is optionally substituted with from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C₁-C₄alkyl and C₁-C₄alkoxy; R₂ is H, C₁-C₄alkyl

(optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₃ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₃ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₂ or R₄ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₄ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₃ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₅ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₆ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms),

285

C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₇ is H or C₁-C₄alkyl; R₈ is H or C₁-C₄alkyl; R₉ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; and R₁₀ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N-ethyl-N-benzyl-4-piperidinamine is excluded;

a compound of formula (IB):

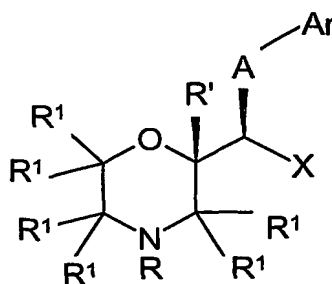


(IB)

wherein Rx is H; Ry is H or C₁-C₄ alkyl; each Rz is independently H or C₁-C₄ alkyl; X represents O; Y represents OH or OR; R is C₁-C₄ alkyl; Ar₁ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); and Ar₂ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl) and halo; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;

a compound of formula (IC)

286

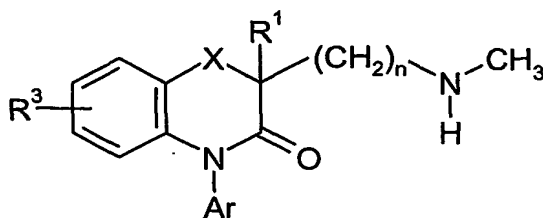


(IC)

wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl),

- 5 S(C₁-C₄ alkyl), halo, hydroxy, CO₂(C₁-C₄ alkyl), pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); a C₁-C₄ alkyl group; a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group; R' is H or C₁-C₄ alkyl; each R¹ is independently H or C₁-C₄ alkyl; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C₁-C₄ alkyl group, a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group;

a compound of formula (ID)

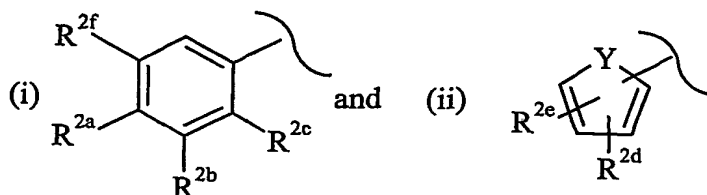


(ID)

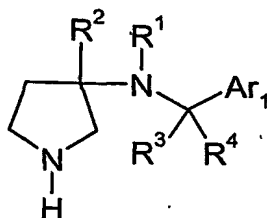
wherein -X- is -C(R⁴R⁵)-, -O- or -S-; n is 2 or 3; R¹ is H or C₁-C₄ alkyl; R³ is H, halo, C₁-C₄ alkyl, O(C₁-C₄ alkyl), nitrile, phenyl or substituted phenyl; R⁴ and R⁵ are each independently selected from H or C₁-C₄ alkyl; Ar- is selected from the group consisting

20 of

287

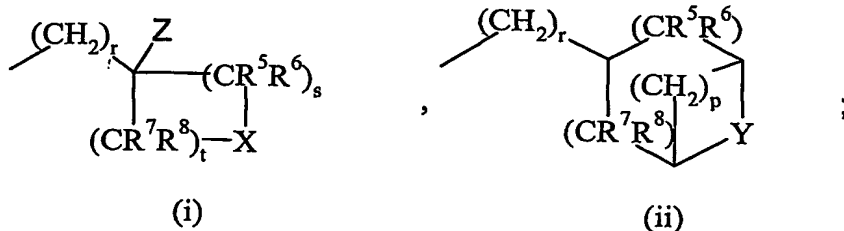


- in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2c} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; -Y- is -O-, -S- or -N(R^6)-; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;
- 5 a compound of formula (IE)



(IE)

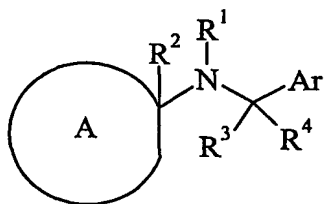
- wherein R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)



- R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl;
- wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally

288

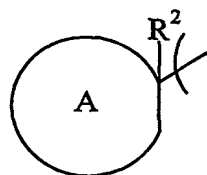
- substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents);
- 5 and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl,
- 10 wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof;
- provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; (d) when -Y- is -O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile is excluded;
- 20 a compound of formula (IF)



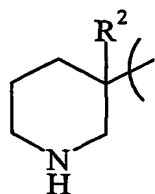
(IF)

wherein

289

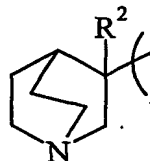


is a group of formula (a) or (b)



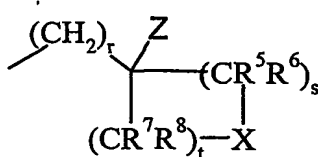
(a)

or

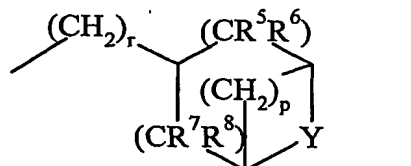


(b)

R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)



(i)



(ii)

R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents), benzyl and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3

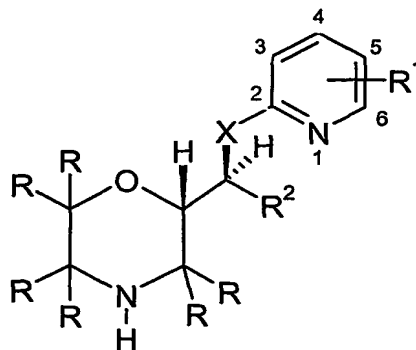
290

substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said

5 naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof;

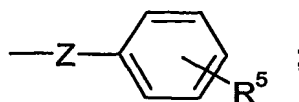
10 provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; and (d) when -Y- is -O- then p cannot be 0; and

a compound of formula (IG)



(IG)

wherein -X- is -S- or -O-; each R is independently selected from H or C₁-C₄ alkyl; R¹ is H, C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, trifluoromethyl, trifluoromethoxy, -NR³R⁴, -CONR³R⁴, -COOR³ or a group of the formula (i)



(i)

20 R² is C₁-C₄ alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁶R⁷, -CONR⁶R⁷, COOR⁶, -

291

$\text{SO}_2\text{NR}^6\text{R}^7$ and $-\text{SO}_2\text{R}^6$; R^5 is selected from C_1 - C_4 alkyl, C_1 - C_4 alkoxy, carboxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, $-\text{NR}^8\text{R}^9$, $-\text{CONR}^8\text{R}^9$, $-\text{SO}_2\text{NR}^8\text{R}^9$ and $-\text{SO}_2\text{R}^8$; R^3 , R^4 , R^6 , R^7 , R^8 and R^9 are each independently selected from H or C_1 - C_4 alkyl; and $-\text{Z}-$ is a bond, $-\text{CH}_2-$, or $-\text{O}-$;

5 or a pharmaceutically acceptable salt thereof.

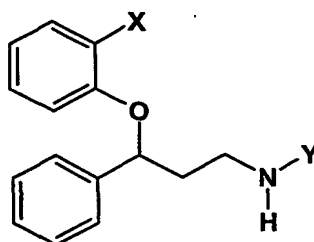
2. Use of a norepinephrine reuptake inhibitor selected from the group consisting of:

atomoxetine or a pharmaceutically acceptable salt thereof;

10 racemic reboxetine or a pharmaceutically acceptable salt thereof;

(S,S) reboxetine or a pharmaceutically acceptable salt thereof;

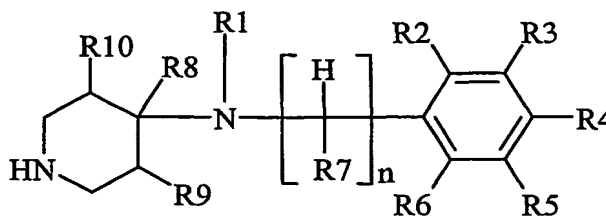
a compound of formula (I):



(I)

15 wherein X is C_1 - C_4 alkylthio, and Y is C_1 - C_2 alkyl, or a pharmaceutically acceptable salt thereof;

a compound of formula (IA):



(IA)

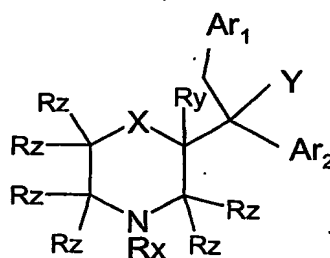
20 wherein n is 1, 2 or 3; R^1 is C_2 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_3 - C_8 cycloalkyl or C_4 - C_{10} cycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally

substituted by an O-C or C=C bond and wherein each group is optionally substituted with from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C₁-C₄alkyl and C₁-C₄alkoxy; R₂ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₃ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₃ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₂ or R₄ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R₄ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy) or -CO₂(C₁-C₄alkyl), or together with R₃ forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy).

293

C₄alkyl and C₁-C₄alkoxy); R₅ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₆ is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R₇ is H or C₁-C₄alkyl; R₈ is H or C₁-C₄alkyl; R₉ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; and R₁₀ is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N-ethyl-N-benzyl-4-piperidinamine is excluded;

a compound of formula (IB):

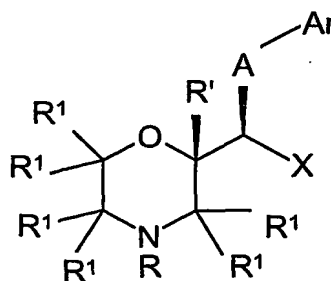


(IB)

wherein R_x is H; R_y is H or C₁-C₄ alkyl; each R_z is independently H or C₁-C₄ alkyl; X represents O; Y represents OH or OR; R is C₁-C₄ alkyl; Ar₁ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl), S(C₁-C₄ alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); and Ar₂ is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl) and halo; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;

a compound of formula (IC)

294



(IC)

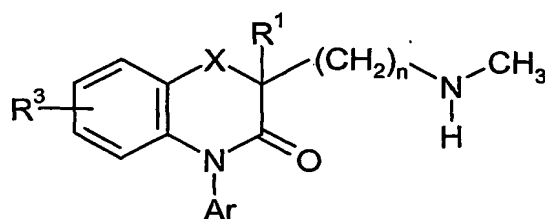
wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C₁-C₄ alkyl, O(C₁-C₄ alkyl),

5 S(C₁-C₄ alkyl), halo, hydroxy, CO₂(C₁-C₄ alkyl), pyridyl, thiophenyl and phenyl

optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄ alkyl); a C₁-C₄ alkyl group; a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl)

10 group; R' is H or C₁-C₄ alkyl; each R¹ is independently H or C₁-C₄ alkyl; wherein each above-mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C₁-C₄ alkyl group, a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group;

a compound of formula (ID)

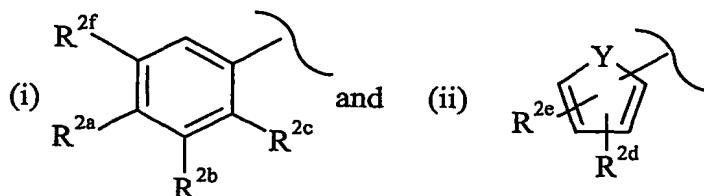


(ID)

wherein -X- is -C(R⁴R⁵)-, -O- or -S-; n is 2 or 3; R¹ is H or C₁-C₄ alkyl; R³ is H, halo, C₁-C₄ alkyl, O(C₁-C₄ alkyl), nitrile, phenyl or substituted phenyl; R⁴ and R⁵ are each independently selected from H or C₁-C₄ alkyl; Ar- is selected from the group consisting

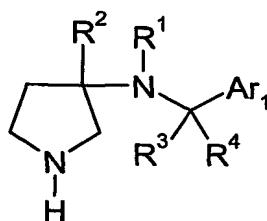
20 of

295



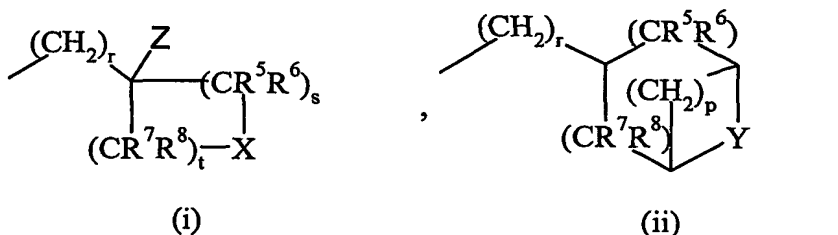
in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2c} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; -Y- is -O-, -S- or -N(R^6)-; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;

a compound of formula (IE)



(IE)

wherein R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)

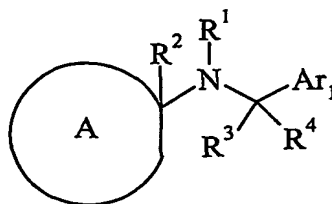


R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally

substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents);

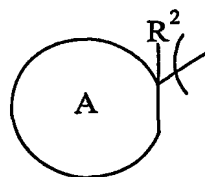
- 5 and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, 10 wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three 15 carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; (d) when -Y- is -O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile is excluded;

20 a compound of formula (IF)

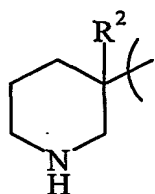


(IF)

wherein

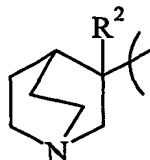


is a group of formula (a) or (b)



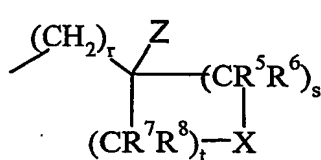
(a)

or

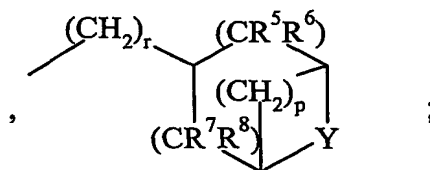


(b)

R^1 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C_3 - C_6 cycloalkyl), -SO₂-(C_1 - C_3 alkyl), -CN, -COO-(C_1 - C_2 alkyl) and -OH); C_2 - C_6 alkenyl; -(CH₂)_q-Ar₂; or a group of formula (i) or (ii)



(i)



(ii)

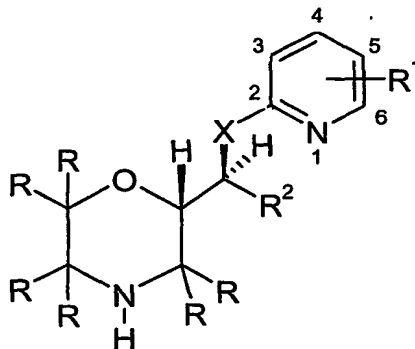
R^2 , R^3 and R^4 are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1 - C_2 alkyl; -X- is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or -O-(C_1 - C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1 - C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C_1 - C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents), benzyl and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3

substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said

5 naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three

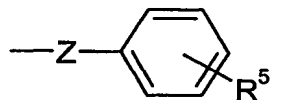
10 carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C₁-C₃ alkyl), then -X- is -CH₂-; and (d) when -Y- is -O- then p cannot be 0; and

a compound of formula (IG)



(IG)

wherein -X- is -S- or -O-; each R is independently selected from H or C₁-C₄ alkyl; R¹ is H, C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, trifluoromethyl, trifluoromethoxy, -NR³R⁴, -CONR³R⁴, -COOR³ or a group of the formula (i)



(i)

20 R² is C₁-C₄ alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-C₄ alkyl, C₁-C₄ alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, -NR⁶R⁷, -CONR⁶R⁷, COOR⁶, -

$\text{SO}_2\text{NR}^6\text{R}^7$ and $-\text{SO}_2\text{R}^6$; R^5 is selected from C_1 - C_4 alkyl, C_1 - C_4 alkoxy, carboxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, $-\text{NR}^8\text{R}^9$, $-\text{CONR}^8\text{R}^9$, $-\text{SO}_2\text{NR}^8\text{R}^9$ and $-\text{SO}_2\text{R}^8$; R^3 , R^4 , R^6 , R^7 , R^8 and R^9 are each independently selected from H or C_1 - C_4 alkyl; and -Z- is a bond, $-\text{CH}_2-$, or $-\text{O}-$;

5 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a Pervasive Developmental Disorder.

3. The method of claim 1 or the use of claim 2, wherein said Pervasive Developmental Disorder is selected from the group consisting of Autistic Disorder,
10 Asperger's Disorder, Rett's Disorder, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder Not Otherwise Specified.

4. The method of claim 1 or 3, or the use of claim 2 or 3, wherein said selective norepinephrine reuptake inhibitor is atomoxetine hydrochloride.